

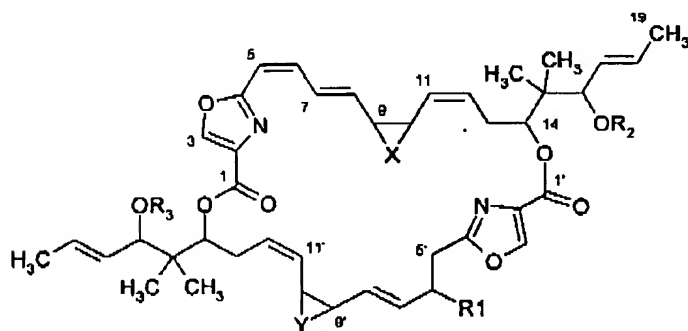
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AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in this application:

Listing of claims:

1. (Currently Amended) A disorazole derivative compound of the general formula I



Formula I

in which independently of one another

R1 is:

- (i) hydrogen,
- (ii) OR4,
- (iii) part of a double bond to C5',

R2, R3 and R4 are:

- (i) hydrogen,
- (ii) unsubstituted or substituted (C₁-C₆)-alkyl,
- (iii) (C₁-C₄)-alkyl substituted by one or more fluorine atoms, preferably a trifluoromethyl group,
- (iv) unsubstituted or substituted (C₁-C₄)-alkyl-(C₆-C₁₄)-aryl, unsubstituted or substituted (C₁-C₄)-alkyl-heteroaryl

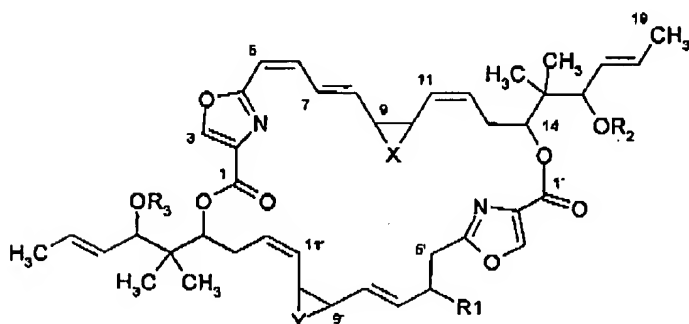
- (v) (C₁-C₄)-alkoxycarbonyl, (C₁-C₄)-alkylaminocarbonyl (C₁-C₄)-alkylaminothiocarbonyl, (C₁-C₆)-alkyl-carbonyl or (C₁-C₆)-alkoxycarbonyl-(C₁-C₆)-alkyl,
 it being possible for the substitution of the alkyl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, NH-(C₃-C₁₂)-cycloalkyl, OH, O-(C₁-C₂₀)-alkyl to take place singly or, on identical or different atoms, multiply by identical or different substituents, and it being possible for the substitution of an aryl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, OH, O-(C₁-C₂₀)-alkyl and/or (C₃-C₈)-heterocyclyl having 1 to 5 heteroatoms, preferably nitrogen, oxygen, sulfur to take place singly or, on identical or different atoms, multiply by identical or different substituents,

and

X, Y are: in each case individually independently of one another or together oxygen, sulfur, two vicinal hydroxyl groups, two vicinal methoxy groups, part of a double bond,
with the proviso that disorazole A1 (in which R1 is methoxy, R2 and R3 are hydrogen, X is oxygen and Y is the part of a double bond), disorazole F2 (in which R1 is hydroxyl, R2 and R3 are hydrogen, X is the part of a double bond and Y is the part of a double bond) and disorazole E (in which R1 is methoxy, R2, R3 are hydrogen, X is oxygen and Y is oxygen) are excluded a compound being excluded in which R1 is methoxy, R2, R3 are hydrogen, X is oxygen and Y is the part of a double bond,

its tautomers, E/Z isomers, stereoisomers, including the diastereomers and enantiomers, and the physiologically tolerable salts thereof.

2. (Previously Presented) The compound of claim 1, wherein R1 and R2 are hydrogen, R3 is methyl and X and Y are oxygen.
3. (Currently Amended) A pharmaceutical composition comprising a disorazole derivative compound of the general formula I formula Ia



Formula Ia

in which independently of one another

R1 is:

- (i) hydrogen,
- (ii) OR₄,
- (iii) part of a double bond to C5',

R2, R3 and R4 are:

- (i) hydrogen,
- (ii) unsubstituted or substituted (C₁-C₆)-alkyl,

- (iii) (C₁-C₄)-alkyl substituted by one or more fluorine atoms, preferably a trifluoromethyl group,
- (iv) unsubstituted or substituted (C₁-C₄)-alkyl-(C₆-C₁₄)-aryl, unsubstituted or substituted (C₁-C₄)-alkyl-heteroaryl,
- (v) (C₁-C₄)-alkoxycarbonyl, (C₁-C₄)-alkylaminocarbonyl (C₁-C₄)-alkylaminothiocarbonyl, (C₁-C₆)-alkyl-carbonyl or (C₁-C₆)-alkoxycarbonyl-(C₁-C₆)-alkyl,

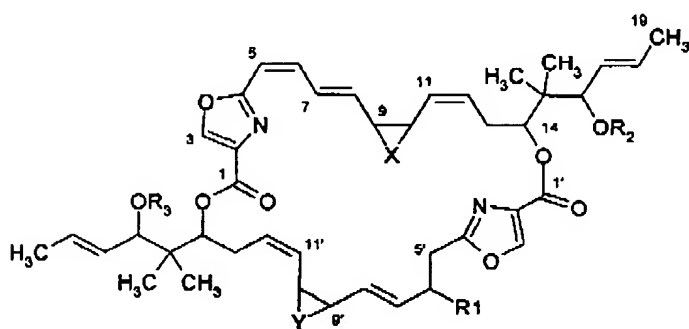
it being possible for the substitution of the alkyl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, NH-(C₃-C₁₂)-cycloalkyl, OH, O-(C₁-C₂₀)-alkyl to take place singly or, on identical or different atoms, multiply by identical or different substituents, and it being possible for the substitution of an aryl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, OH, O-(C₁-C₂₀)-alkyl and/or (C₃-C₈)-heterocyclyl having 1 to 5 heteroatoms, preferably nitrogen, oxygen, sulfur to take place singly or, on identical or different atoms, multiply by identical or different substituents,

and

X, Y are: in each case individually independently of one another or together oxygen, sulfur, two vicinal hydroxyl groups, two vicinal methoxy groups, part of a double bond,
~~a with the proviso that the compound being excluded~~ in which R₁ is methoxy, R₂, R₃ are hydrogen, X is oxygen and Y is the part of a double bond is excluded.

its tautomers, E/Z isomers, stereoisomers, including the diastereomers and enantiomers, and the physiologically tolerable salts thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

4. (Currently Amended) A method for the treatment of oncoses comprising administering the a compound of claim 1 of the general formula Ia



Formula Ia

in which independently of one another

R1 is:

- (iv) hydrogen,
- (v) OR4,
- (vi) part of a double bond to C5',

R2, R3 and R4 are:

- (vi) hydrogen,
- (vii) unsubstituted or substituted (C₁-C₆)-alkyl,
- (viii) (C₁-C₄)-alkyl substituted by one or more fluorine atoms, preferably a trifluoromethyl group,

- (ix) unsubstituted or substituted (C₁-C₄)-alkyl-(C₆-C₁₄)-aryl, unsubstituted or substituted (C₁-C₄)-alkyl-heteroaryl,
- (x) (C₁-C₄)-alkoxycarbonyl, (C₁-C₄)-alkylaminocarbonyl (C₁-C₄)-alkylaminothiocarbonyl, (C₁-C₆)-alkyl-carbonyl or (C₁-C₆)-alkoxycarbonyl-(C₁-C₆)-alkyl,
- it being possible for the substitution of the alkyl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, NH-(C₃-C₁₂)-cycloalkyl, OH, O-(C₁-C₂₀)-alkyl to take place singly or, on identical or different atoms, multiply by identical or different substituents, and it being possible for the substitution of an aryl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, OH, O-(C₁-C₂₀)-alkyl and/or (C₃-C₈)-heterocyclyl having 1 to 5 heteroatoms, preferably nitrogen, oxygen, sulfur to take place singly or, on identical or different atoms, multiply by identical or different substituents,

and

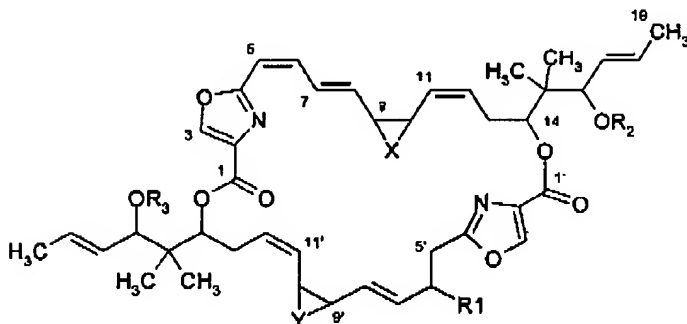
X, Y are: in each case individually independently of one another or together oxygen, sulfur, two vicinal hydroxyl groups, two vicinal methoxy groups, part of a double bond,

a with the proviso that the compound being excluded in which R₁ is methoxy, R₂, R₃ are hydrogen, X is oxygen and Y is the part of a double bond is excluded,

its tautomers, E/Z isomers, stereoisomers, including the diastereomers and enantiomers, and the physiologically tolerable salts thereof,

to an individual in need of such treatment alone or in combination with a cytotoxic substance and/or an inhibitor of signal transduction.

5. (Currently Amended) A method for the treatment of a disease in humans or animals which is based on the rapid and uncontrolled proliferation of endogenous cells comprising administering ~~the~~ a compound of claim 1 of the general formula Ia



Formula Ia

in which independently of one another

R1 is:

- (vii) hydrogen,
- (viii) OR4,
- (ix) part of a double bond to C5',

R2, R3 and R4 are:

- (xi) hydrogen,
- (xii) unsubstituted or substituted (C₁-C₆)-alkyl,

- (xiii) (C₁-C₄)-alkyl substituted by one or more fluorine atoms, preferably a trifluoromethyl group,
- (xiv) unsubstituted or substituted (C₁-C₄)-alkyl-(C₆-C₁₄)-aryl, unsubstituted or substituted (C₁-C₄)-alkyl-heteroaryl,
- (xv) (C₁-C₄)-alkoxycarbonyl, (C₁-C₄)-alkylaminocarbonyl (C₁-C₄)-alkylaminothiocarbonyl, (C₁-C₆)-alkyl-carbonyl or (C₁-C₆)-alkoxycarbonyl-(C₁-C₆)-alkyl,
it being possible for the substitution of the alkyl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, NH-(C₃-C₁₂)-cycloalkyl, OH, O-(C₁-C₂₀)-alkyl to take place singly or, on identical or different atoms, multiply by identical or different substituents, and it being possible for the substitution of an aryl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, OH, O-(C₁-C₂₀)-alkyl and/or (C₃-C₈)-heterocyclyl having 1 to 5 heteroatoms, preferably nitrogen, oxygen, sulfur to take place singly or, on identical or different atoms, multiply by identical or different substituents,

and

X, Y are: in each case individually independently of one another or together oxygen, sulfur, two vicinal hydroxyl groups, two vicinal methoxy groups, part of a double bond,

a with the proviso that the compound in which R1 is methoxy, R2, R3 are hydrogen, X is oxygen and Y is the part of a double bond is excluded,

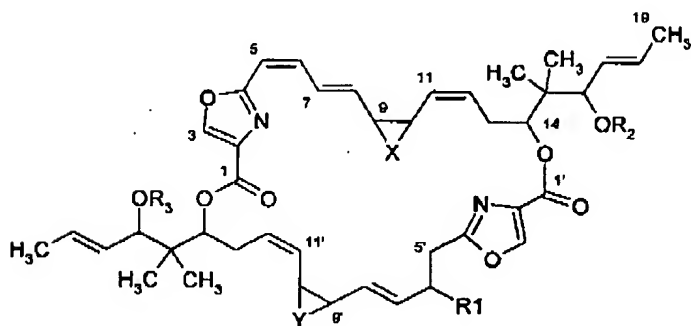
its tautomers, E/Z isomers, stereoisomers, including the diastereomers and enantiomers, and the physiologically tolerable salts thereof, to a human or animal in need of such treatment.

6. (Cancelled)

7. (Cancelled)

8. (Cancelled)

9. (Currently Amended) A method for the treatment of benign or malignant oncoses in humans or animals comprising administering the ~~a~~ compound of claim 1 the general formula Ia



Formula Ia

in which independently of one another

R1 is:

- (x) hydrogen,
- (xi) OR4,
- (xii) part of a double bond to C5',

R2, R3 and R4 are:

- (xvi) hydrogen,
- (xvii) unsubstituted or substituted (C₁-C₆)-alkyl,
- (xviii) (C₁-C₄)-alkyl substituted by one or more fluorine atoms, preferably a trifluoromethyl group,
- (xix) unsubstituted or substituted (C₁-C₄)-alkyl-(C₆-C₁₄)-aryl, unsubstituted or substituted (C₁-C₄)-alkyl-heteroaryl,
- (xx) (C₁-C₄)-alkoxycarbonyl, (C₁-C₄)-alkylaminocarbonyl (C₁-C₄)-alkylaminothiocarbonyl, (C₁-C₆)-alkyl-carbonyl or (C₁-C₆)-alkoxycarbonyl-(C₁-C₆)-alkyl,
it being possible for the substitution of the alkyl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, NH-(C₃-C₁₂)-cycloalkyl, OH, O-(C₁-C₂₀)-alkyl to take place singly or, on identical or different atoms, multiply by identical or different substituents, and it being possible for the substitution of an aryl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, OH, O-(C₁-C₂₀)-alkyl and/or (C₃-C₈)-heterocyclyl having 1 to 5 heteroatoms, preferably nitrogen, oxygen, sulfur to take place singly or, on identical or different atoms, multiply by identical or different substituents,

and

X, Y are: in each case individually independently of one another or together oxygen, sulfur, two vicinal hydroxyl groups, two vicinal methoxy groups, part of a double bond,
with the proviso that the compound in which R₁ is methoxy, R₂, R₃ are hydrogen, X is oxygen and Y is the part of a double bond is excluded,

its tautomers, E/Z isomers, stereoisomers, including the diastereomers and enantiomers, and the physiologically tolerable salts thereof to a human or animal in need of such treatment.

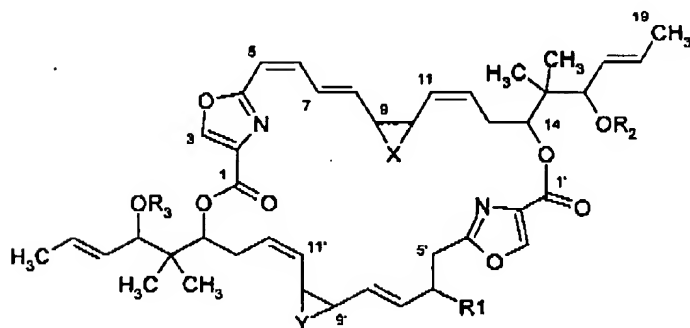
10. (Previously Presented) The method as claimed in claim 9 wherein the oncos is breast cancer, ovarian cancer, lung cancer, skin cancer, prostate cancer, renal cell cancer, hepatic cancer, pancreatic cancer, colonic cancer or brain cancer in humans.
11. (Currently Amended) The method of claim 9, wherein the compound of ~~claim 1~~ formula Ia is administered in combination with ~~another~~ another antitumor agent.
12. (Currently Amended) The method of claim 9, wherein the compound of ~~claim 1~~ formula Ia is administered in combination with paclitaxel, docetaxel, vincristine, vindesine, cisplatin, carboplatin, doxorubicin, ifosfamide, cyclophosphamide, 5-FU, methotrexate or in combination with an immunomodulator or antibody or in combination with a signal transduction inhibitor.
13. (Currently Amended) The method of claim 12, wherein the signal transduction inhibitor is Herceptin, Glivec or Iressa.
14. (Previously Presented) The pharmaceutical composition of claim 3, which is in the form of a solution, suspension, emulsion, foam, ointment, paste, patch or implant.

15. (Cancelled)

16. (Cancelled)

17. (Cancelled)

18. (New) A method for the treatment of a tumor disease selected from the group consisting of sarcoma, adenocarcinoma, melanoma, lymphoma, leukemia, non Hodgkin's lymphoma, Hodgkin's disease, breast cancer, ovarian cancer, transitional cell bladder carcinoma, small cell lung cancer, multiple myeloma, kaposi's sarcoma, cervical cancer, pancreatic cancer, testicular carcinoma, prostate cancer, hepatic cancer, renal cancer, skin cancer, cancers of the brain, acute lymphatic leukemia (ALL), acute promyelocytic leukemia (APL), rhabdomyo sarcoma, euroblastoma, Wilm's tumor, medulloblastoma, choriocarcinoma, and non-small cell lung cancer, cervical carcinoma, ovarian adenocarcinoma, glioblastoma, lung carcinoma, breast cancer, melanoma, colon cancer and blood cancer, comprising administering a disorazole compound of the general formula Ia:



Formula Ia

in which independently of one another

R1 is:

- (xiii) hydrogen,
- (xiv) OR4,
- (xv) part of a double bond to C5',

R2, R3 and R4 are:

- (xxi) hydrogen,
- (xxii) unsubstituted or substituted (C₁-C₆)-alkyl,
- (xxiii) (C₁-C₄)-alkyl substituted by one or more fluorine atoms, preferably a trifluoromethyl group,
- (xxiv) unsubstituted or substituted (C₁-C₄)-alkyl-(C₆-C₁₄)-aryl, unsubstituted or substituted (C₁-C₄)-alkyl-heteroaryl,
- (xxv) (C₁-C₄)-alkoxycarbonyl, (C₁-C₄)-alkylaminocarbonyl (C₁-C₄)-alkylaminothiocarbonyl, (C₁-C₆)-alkyl-carbonyl or (C₁-C₆)-alkoxycarbonyl-(C₁-C₆)-alkyl,

it being possible for the substitution of the alkyl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, NH-(C₃-C₁₂)-cycloalkyl, OH, O-(C₁-C₂₀)-alkyl to take place singly or, on identical or different atoms, multiply by identical or different substituents, and it being possible for the substitution of an aryl radical by F, Cl, Br, I, CN, NH₂, NH-(C₁-C₂₀)-alkyl, OH, O-(C₁-C₂₀)-alkyl and/or (C₃-C₈)-heterocyclyl having 1 to 5 heteroatoms, preferably nitrogen, oxygen, sulfur to take place singly or, on identical or different atoms, multiply by identical or different substituents,

and

X, Y are: in each case individually independently of one another or together oxygen, sulfur, two vicinal hydroxyl groups, two vicinal methoxy groups, part of a double bond,

with the proviso that the compound in which R1 is methoxy, R2, R3 are hydrogen, X is oxygen and Y is the part of a double bond is excluded, its tautomers, E/Z isomers, stereoisomers, including the diastereomers and enantiomers, and the physiologically tolerable salts thereof, to an individual in need of such treatment alone or in combination with a cytotoxic substance and/or an inhibitor of signal transduction.